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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,879	11/20/2000	Tatsuya Tamura	TAMURA-5	4195

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/700,879	TAMURA ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-12,17,18 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-12,17,18 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1, 3, 5-12, 17, 18, 22-25 are pending. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any rejection or objection not expressly repeated has been withdrawn.

Claim Rejections - 35 USC § 103

Claims 1, 5, 8, 12, 23, and 24 are again rejected under 35 U.S.C. 103(a) as being unpatentable over AKIMA et al (US 5,733,891), as set forth in the previous Office action.

The invention is as set forth in the previous Office action.

Applicant's arguments filed April 26, 2005 have been fully considered but they are not persuasive.

Applicant contends that in the AKIMA compound "hyaluronic acid merely acts as a carrier and not as an active agent which acts synergistically with the medicinal ingredient." However, Applicant has presented no evidence for any synergistic effect seen with the claimed compounds.

Applicant further discusses the fact that daunomycin is not a therapeutic agent for joint disorders. This was clearly acknowledged in the Office action. Applicant will note that the rejection is one of obviousness, not anticipation. Applicant further argues that AKIMA identifies prednisolone as a hormonal anti-cancer agent, so that one of ordinary would not be motivated to use a conjugate of HA and prednisolone to treat joint disorders. Neither the reference's intended

use for this suggested compound nor its identification as a "pro-drug" is of import. The examiner maintains that for one of ordinary skill in possession of the reference, it would be obvious to prepare a prednisolone-linker-HA conjugate. The examiner agrees that there is no motivation for the treatment of joint disorders in this reference. However, the examiner notes that none of the claims rejected over AKIMA alone are method claims.

Applicant argues that the reference uses a spacer "in order to overcome the difficulty of dissolving hyaluronic acid in an organic solvent." That AKIMA may have a different intention in using the spacer does not appear to be germane. The suggestion to prepare the conjugates using any of the named agents remains the same. Further regarding the spacer, Applicant notes that "[o]nly Example 2 provides a disclosure relating to a spacer; the other examples disclose that hyaluronic acid directly bonds to the medicinal ingredient." (Original emphasis) The reference does indeed teach conjugates with and without spacers. The examiner does not find that the addition of the latter lessens validity of the teaching of the former.

Applicant further argues that the AKIMA compound would be expected migrate to regional lymph nodes and decompose to release the medicinal ingredient and not be retained without dissociation at the treatment site to produce the desired synergistic effect. Again, Applicant appears to have conflated the product and method of use rejections. These claims are drawn to compounds having no functional limitation regarding its activity *in vivo*. Again, Applicant has supplied no evidence for synergism.

Claims 1, 3, 5-10, 12, 18, 23, and 24 are again rejected under 35 U.S.C. 103(a) as being unpatentable over AKIMA et al (US 5,733,891) and GALLARDY et al (WO 92/09563), as set forth in the previous Office action.

The invention is as set forth in the previous Office action.

Applicant's arguments filed April 26, 2005 have been fully considered but they are not persuasive.

Applicant argues that GALLARDY does not provide specific examples of conjugates. The examiner agrees. However, maintains it would be obvious to modify the HA conjugates taught by AKIMA by substituting any anti-cancer agent, such as an MMP inhibitor, such as those taught by GALLARDY, with a reasonable expectation of success. The artisan would be motivated to prepare such a conjugate or pharmaceutical composition thereof for the art disclosed utility of cancer treatment.

Claims 1, 3, 5-12, 17, 18, and 22-25 are again rejected under 35 U.S.C. 103(a) as being unpatentable over PRESTWICH et al (US 5,874,417) in view of AKIMA et al (US 5,733,891) and GALLARDY et al (WO 92/09563), as set forth in the previous Office action.

The invention is as set forth in the previous Office action.

Applicant's arguments filed April 26, 2005 have been fully considered but they are not persuasive.

Citing a passage from the reference, Applicant argues that "Prestwich teaches that the essential feature of Prestwich's invention resides in crosslinking of hyaluronic acid via linkage and takes advantage of the chemical nature specific to hydrazide." The examiner does not agree

with this interpretation of this passage. The examiner notes that included in this passage is "[i]t is therefore yet another object ... to provide an HA derivative utilizing hydrazides in which the character of the HA is not compromised, i.e., significantly changed ..." From this, one of ordinary skill would reasonably surmise that the reference is teaching an alternative method of preparing HA conjugates, but that HA-drug conjugates would have similar utility regardless of the precise physical attachment of the drug to HA.

Applicant further contends that "hyaluronic acid or hyaluronic acid derivative in the conjugate disclosed in Prestwich can merely be used as carrier for drug delivery to release a variety of drugs." The examiner agrees. Specifically, the reference teaches drug delivery for joint therapy.

Finally, Applicant argues that the reference does not recognize either (1) that both the therapeutic agent and the HA exhibit their own effects for the treatment of joint disease or (2) that they exhibit synergistic effects. Regarding (1), the fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Regarding (2), again Applicant has supplied no evidence for synergism.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more. Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
July 1, 2005